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STRUCTURE FILE UPDATES: 16 SEP 2005 HIGHEST RN 863378-74-9  
 DICTIONARY FILE UPDATES: 16 SEP 2005 HIGHEST RN 863378-74-9

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH JULY 14, 2005

Please note that search-term pricing does apply when conducting SmartSELECT searches.

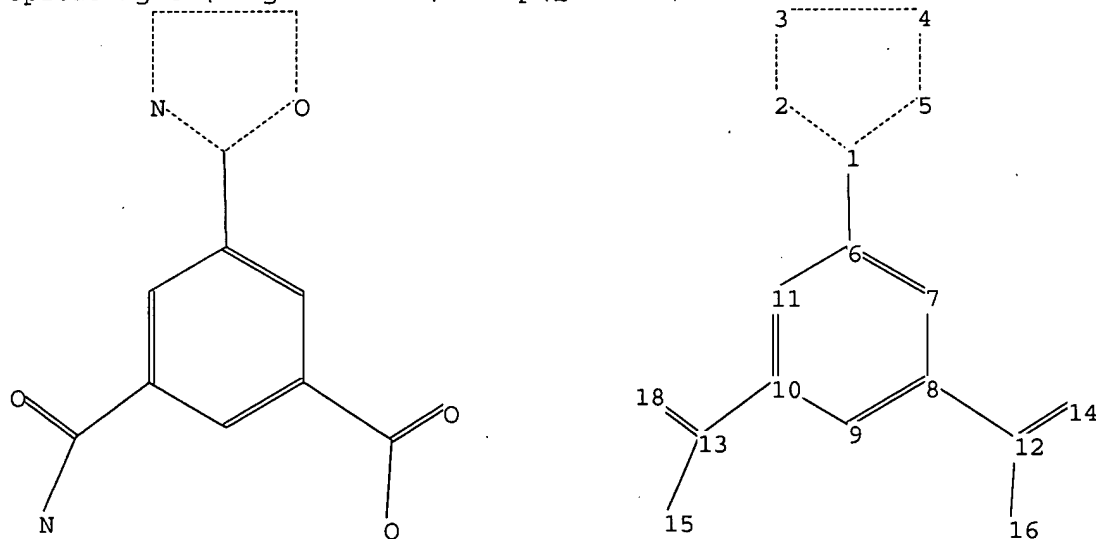
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*****
*
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added,   *
* effective March 20, 2005. A new display format, IDERL, is now    *
* available and contains the CA role and document type information. *
*
*****
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Structure search iteration limits have been increased. See HELP SLIMITS for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:  
<http://www.cas.org/ONLINE/DBSS/registryss.html>

=>

Uploading C:\Program Files\Stnexp\Queries\10600100.str



chain nodes :

12 13 14 15 16 18

ring nodes :

1 2 3 4 5 6 7 8 9 10 11

chain bonds :

1-6 8-12 10-13 12-14 12-16 13-15 13-18

ring bonds :  
 1-2 1-5 2-3 3-4 4-5 6-7 6-11 7-8 8-9 9-10 10-11  
 exact/norm bonds :  
 1-2 1-5 2-3 3-4 4-5 12-14 12-16 13-15 13-18  
 exact bonds :  
 1-6 8-12 10-13  
 normalized bonds :  
 6-7 6-11 7-8 8-9 9-10 10-11  
 isolated ring systems :  
 containing 1 : 6 :

Match level :

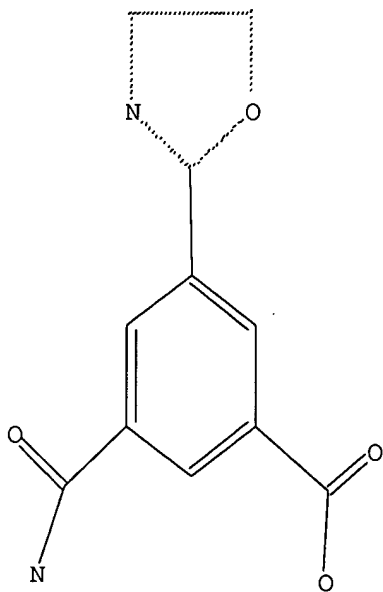
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom  
 11:Atom 12:CLASS 13:CLASS 14:CLASS 15:CLASS 16:CLASS 18:CLASS

L1 STRUCTURE UPLOADED

=> d

L1 HAS NO ANSWERS

L1 STR



Structure attributes must be viewed using STN Express query preparation.

=> s 11

SAMPLE SEARCH INITIATED 09:25:24 FILE 'REGISTRY'  
 SAMPLE SCREEN SEARCH COMPLETED - 86 TO ITERATE

100.0% PROCESSED 86 ITERATIONS  
 SEARCH TIME: 00.00.01

1 ANSWERS

FULL FILE PROJECTIONS: ONLINE \*\*COMPLETE\*\*

10600100 09/15/05

BATCH \*\*COMPLETE\*\*  
PROJECTED ITERATIONS: 1164 TO 2276  
PROJECTED ANSWERS: 1 TO 80

L2 1 SEA SSS SAM L1

=> s l1 full  
FULL SEARCH INITIATED 09:25:47 FILE 'REGISTRY'  
FULL SCREEN SEARCH COMPLETED - 1552 TO ITERATE

100.0% PROCESSED 1552 ITERATIONS 26 ANSWERS  
SEARCH TIME: 00.00.01

L3 26 SEA SSS FUL L1

=> file caplus  
COST IN U.S. DOLLARS SINCE FILE TOTAL  
ENTRY SESSION  
FULL ESTIMATED COST 161.33 161.54

FILE 'CAPLUS' ENTERED AT 09:25:52 ON 18 SEP 2005  
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.  
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FILE COVERS 1907 - 18 Sep 2005 VOL 143 ISS 13  
FILE LAST UPDATED: 16 Sep 2005 (20050916/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s l3  
L4 4 L3  
=> d ibib abs hitstr tot

L4 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2005 ACS ON STN

ACCESSION NUMBER: 2005:472134 CAPLUS

DOCUMENT NUMBER: 143:26648

TITLE: Preparation of macrocyclic lactams for treatment of neurological or vascular disorders related to  $\beta$ -amyloid generation and/or aggregation

INVENTOR(S): Auberson, Yves; Betschart, Claudia; Glatthar, Ralf; Laumen, Kurt; Machauer, Rainer; Tintelnot-Blomley, Marina; Troxler, Thomas J.; Veenstra, Siem Jacob

PATENT ASSIGNEE(S): Novartis A.-G., Switz.; Novartis Pharma G.m.b.H.

SOURCE: PCT Int. Appl., 84 pp.

CODEN: PIXXDZ

Patent

DOCUMENT TYPE:

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

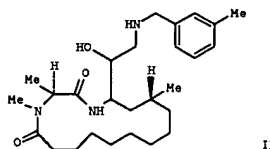
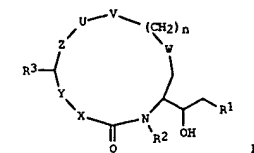
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005049585	A1	20050602	WO 2004-EP12497	20041104
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RW:	BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, FL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
PRIORITY APPL. INFO.:			GB 2003-25830	A 20031105
OTHER SOURCE(S):		MARPAT 143:26648		

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L4 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2005 ACS ON STN

(Continued)



AB The present invention relates to novel macrocyclic compds. of the formula (I) [R1 = each N-(un)substituted CH(Rh)C(O)NH2 or (CH2)kNH2 (wherein k = 0-2); R2 = H, C1-4 alkyl; R3 = H, C1-6 alkyl, (un)substituted C1-6 alkyl-OC(O)NH, C3-7 cycloalkyl-OC(O)NH, C3-7 cycloalkyl-C1-4 alkyl-OC(O)NH, aryl-C1-4 alkyl-OC(O)NH, heteroaryl-C1-4 alkyl-OC(O)NH, C1-4 alkyl-C(O)NH, C3-7 cycloalkyl-C(O)NH, aryl-C(O)NH, aryl-C1-4 alkyl-C(O)NH, heteroaryl-C(O)NH, heteroaryl-C1-4 alkyl-C(O)NH; U = a bond, CF2, CF2CF2, CHF, CHFCHF, cycloprop-1,2-ylene, C1-3 alkyleneoxy, C1-8 alkylene, each (un)substituted NH or an aromatic or heteroarom. ring whereby Z and V are in ortho- or meta-position to each other; V = CH=CH, cycloprop-1,2-ylene, CH2CH(OH), CH(OH)CH2, C(Rh)R(Rh)R(Rh) (wherein Rh = independently H, F, (C1)alkyl); W = C1-6 alkylene, O, S, S(O)2, C(O), C(O)O, OC(O), each (un)substituted NHC(O), C(O)NH, or NH whereby Y and (un)substituted C(O)NH are in meta-position to each other; Y = a bond, O, S(O)2, each (un)substituted S(O)2NH, NHC(O)2, NH, CHOH, C(O)NH, NHC(O), C(O)NHO, or ONHC(O); Z = O, CH2, OF2, CHF, cycloprop-1,2-ylene, a bond; n = 0-5, the number of ring atoms included in the macrocyclic ring being 14, 15, 16 or 17, in free base form or in acid addition salt form]. These compds. are useful as pharmaceuticals for the treatment of neurol. or vascular disorders related to  $\beta$ -amyloid generation and/or aggregation which may include neurodegenerative diseases like Alzheimer's disease, Down's Syndrome, memory and cognitive impairment, dementia, amyloid neuropathies, brain inflammation, nerve and brain trauma, vascular amyloidosis, or cerebral hemorrhage with amyloidosis. They inhibit BACE2 (beta-site APP-cleaving enzyme 2) ( $\beta$ -Secretase 2) or cathepsin D, close homologues of the pepsin-type aspartyl proteases and of  $\beta$ -secretase and can be used for the treatment of disorders involving processing by such enzymes. Particularly they inhibit  $\beta$ -secretase and as such inhibit the generation of  $\beta$ -amyloid and the subsequent

L4 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2005 ACS ON STN (Continued)

aggregation into oligomers and fibrils. Thus ring-closing metathesis of hept-6-enoic acid N-[(S)-1-[(R)-1-(2-chloro-1-hydroxyethyl)-3-methylhept-6-enyl]carbamoyl]ethyl-N-methylamide in the presence of [1,3-bis(2,4,6-trimethylphenyl)-2-imidazolidinylidene]dichloro(phenylmethyl)ene-(tricyclohexylphosphine)ruthenium (Grubbs II catalyst) in CH2Cl2 under refluxing gave (E)-(3S,14R)-16-(2-Chloro-1-hydroxyethyl)-3,4,14-trimethyl-1,4-diazacyclohexadec-10-ene-2,5-dione which was hydrogenated over 10% Pd-C in ethanol to give (3S,14R)-16-(2-Chloro-1-hydroxyethyl)-3,4,14-trimethyl-1,4-diazacyclohexadecane-2,5-dione (II). Cyclization of II by treatment with a mixt. of aq. 1 M NaOH and THF at 0° for 2 h gave (3S,14R)-3,4,14-trimethyl-16-(oxiran-2-yl)-1,4-diazacyclohexadecane-2,5-dione which underwent amination with 3-methylbenzylamine at 65° for 2 h to give (3S,14R)-16-[1-Hydroxy-2-(3-methylbenzylamino)ethyl]-3,4,14-trimethyl-1,4-diazacyclohexadecane-2,5-dione. The compds. II showed inhibitory activity of <20  $\mu$ M in at least one of assays on human BACE, BACE-2, cathepsin D, and cellular release of amyloid peptide 1-40.

IT 852878-66-1P, N-Allyl-N-ethyl-5-(oxazol-2-yl)isophthalamic acid

RI: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

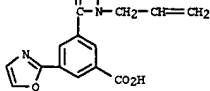
(Intermediate; preparation of macrocyclic lactams for treatment of neurol.

or vascular disorders related to  $\beta$ -amyloid generation and/or aggregation)

RN 852878-66-1 CAPLUS

CN Benzoic acid, 3-[(ethyl-2-propenylamino)carbonyl]-5-(2-oxazolyl)- (9CI)

(CA INDEX NAME)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2005 ACS ON STN

ACCESSION NUMBER: 2004:220301 CAPLUS

DOCUMENT NUMBER: 140:270550

TITLE: A preparation of 1,3-diamino-2-hydroxypropane derivatives as beta-secretase enzyme inhibitors

INVENTOR(S): Fobian, Yvette M.; Freskos, John N.; Jagodzinska, Barbara

PATENT ASSIGNEE(S): Elan Pharmaceuticals, Inc., USA; Pharmacia & Upjohn

SOURCE: PCT Int. Appl., 535 pp.

CODEN: PIXXDZ

Patent

Document Type:

Language:

Family Acc. Num. Count: 1

Patent Information:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004022523	A2	20040318	WO 2003-US28116	20030908
WO 2004022523	A3	20040910		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, GR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, FL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
CA 2497979	AA	20040318	CA 2003-2497979	20030908
US 2004214890	A1	20041028	US 2003-657567	20030908
EP 1534693	A2	20050601	EP 2003-749520	20030908
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK			
BR 2003014071	A	20050705	BR 2003-14071	20030908
PRIORITY APPL. INFO.:			US 2002-408783P	P 20020906
			WO 2003-US28116	W 20030908
OTHER SOURCE(S):		MARPAT 140:270550		

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\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

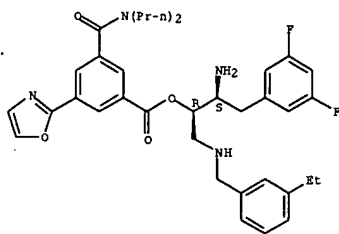
AB The invention relates to diamino(hydroxy)propane derivs. of formula I [wherein: R1 = -(CH2)1-2-S(O)0-2-(C1-6 alkyl) or (un)substituted (cyclo)alkyl, alk(en/yn)yl, (hetero)aryl, etc.; R2 = H, C1-6 alkyl optionally substituted with 1-3 substituents, (CH2)0-4-(hetero)aryl, C2-6 alk(en/yn)yl, etc.; R3 = H, C1-6 alkyl optionally substituted with 1-3 substituents, (CH2)0-4-(hetero)aryl, etc.; R4 = C1-10 alkyl optionally substituted with 1-3 substituents, -(CH2)0-3-cycloalkyl, -(CR7R8)0-4-(hetero)aryl, etc.; one of R5 and R6 is H and the other is -(C(O)(CR9R10)1-6-X-R11, etc.; R7 and R8 are independently selected from H, alkyl, hydroxyalkyl, alk(en/yn)yl, etc.; R9 and R10 are independently selected from H or C1-10 alkyl; R11 = (hetero)aryl, optionally substituted C1-10 alkyl, or C3-8 cycloalkyl, etc.; X = O, S, S(O)2, etc.]. Compds. I include inhibitors of beta-secretase enzyme useful in the treatment of Alzheimer's disease and other diseases characterized by deposition of A beta-peptide in a mammal. Biol. examples include beta-secretase

L4 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)  
inhibition, assays using synthetic oligopeptide-substrates, inhibition of A beta prodn. in human patients, etc. For instance, compd. II (prepn. 8) was prepd. via amidation of benzoic acid deriv. III by diamino(hydroxy)propane deriv. IV and subsequent Boc-cleavage (no yield data). Using 19F-NMR an intramol. acyl-migration was obsd. when compd. II was dissolved in DMSO-d6 and pH 4 buffer soln. was added.

IT 674311-20-7P 674311-21-8P 674311-24-1P  
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)  
(Intermediate; preparation of diamino(hydroxy)propane derivs. useful as beta-secretase inhibitors)

RN 674311-20-7 CAPLUS  
CN Benzoic acid, 3-[(dipropylamino)carbonyl]-5-(2-oxazolyl)-, (1R,2S)-2-amino-3-(3,5-difluorophenyl)-1-[[[3-(ethylphenyl)methyl]amino]methyl]propyl ester, dihydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

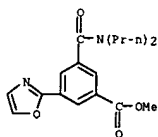


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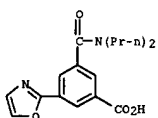
RN 674311-21-8 CAPLUS  
CN Benzoic acid, 3-[(dipropylamino)carbonyl]-5-(2-oxazolyl)-, (1R,2S)-2-amino-3-(3,5-difluorophenyl)-1-[[[1-(3-ethylphenyl)cyclopropyl]amino]methyl]propyl ester, dihydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

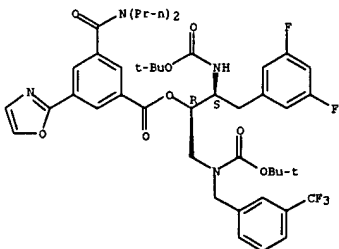


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CN Benzoic acid, 3-[(dipropylamino)carbonyl]-5-(2-oxazolyl)- (9CI) (CA INDEX NAME)



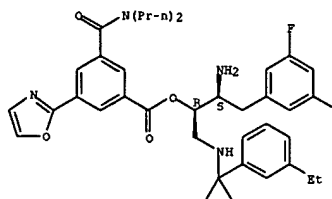
RN 674311-07-0 CAPLUS  
CN Benzoic acid, 3-[(dipropylamino)carbonyl]-5-(2-oxazolyl)-, (1R,2S)-3-(3,5-difluorophenyl)-2-[[[1,1-dimethylethoxy]carbonyl]amino]-1-[[[1,1-dimethylethoxy]carbonyl][3-(trifluoromethyl)phenyl]methyl]amino]methyl]propyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 674311-05-8P  
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP

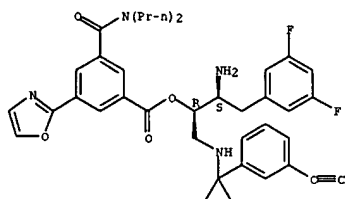
L4 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



● 2 HCl

RN 674311-24-1 CAPLUS  
CN Benzoic acid, 3-[(dipropylamino)carbonyl]-5-(2-oxazolyl)-, (1R,2S)-2-amino-3-(3,5-difluorophenyl)-1-[[[1-(3-ethylphenyl)cyclopropyl]amino]methyl]propyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



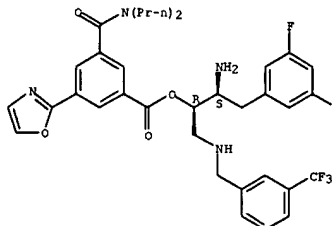
IT 597561-63-2P 597563-26-3P 674311-07-0P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(Intermediate; preparation of diamino(hydroxy)propane derivs. useful as beta-secretase inhibitors)

RN 597561-63-2 CAPLUS  
CN Benzoic acid, 3-[(dipropylamino)carbonyl]-5-(2-oxazolyl)-, methyl ester (9CI) (CA INDEX NAME)

L4 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)  
(Preparation); RACT (Reactant or reagent); USES (Uses)  
(prepn. of diamino(hydroxy)propane derivs. useful as beta-secretase inhibitors)

RN 674311-05-8 CAPLUS  
CN Benzoic acid, 3-[(dipropylamino)carbonyl]-5-(2-oxazolyl)-, (1R,2S)-2-amino-3-(3,5-difluorophenyl)-1-[[[1-(3-(trifluoromethyl)phenyl)methyl]amino]methyl]propyl ester, dihydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



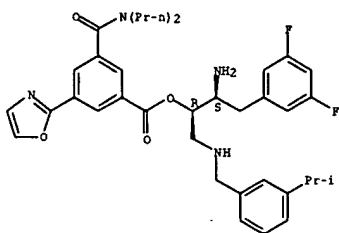
● 2 HCl

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674311-61-6P 674311-64-9P 674311-72-9P  
674311-92-3P  
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(preparation of diamino(hydroxy)propane derivs. useful as beta-secretase inhibitors)

RN 674311-29-6 CAPLUS  
CN Benzoic acid, 3-[(dipropylamino)carbonyl]-5-(2-oxazolyl)-, (1R,2S)-2-amino-3-(3,5-difluorophenyl)-1-[[[1-(3-(1-methylethyl)phenyl)methyl]amino]methyl]propyl ester (9CI) (CA INDEX NAME)

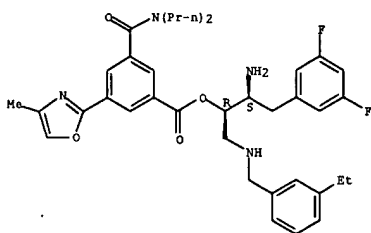
Absolute stereochemistry.

L4 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



RN 674311-31-0 CAPLUS  
 CN Benzoic acid, 3-[(dipropylamino)carbonyl]-5-(4-methyl-2-oxazolyl)-, (1R,2S)-2-amino-3-(3,5-difluorophenyl)-1-[[[3-ethylphenyl)methyl]amino]methyl]propyl ester (9CI) (CA INDEX NAME)

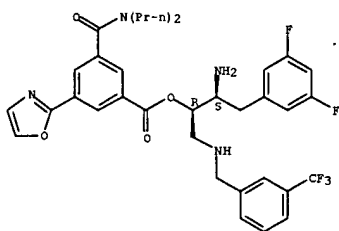
Absolute stereochemistry.



RN 674311-32-1 CAPLUS  
 CN Benzoic acid, 3-[(dipropylamino)carbonyl]-5-(2-oxazolyl)-, (1R,2S)-2-amino-3-(3,5-difluorophenyl)-1-[[[3-(2-methylpropyl)-5-thiazolyl)methyl]amino]methyl]propyl ester (9CI) (CA INDEX NAME)

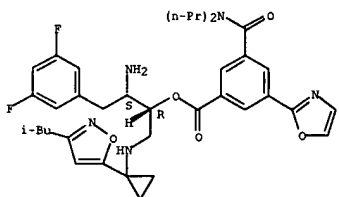
Absolute stereochemistry.

L4 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



RN 674311-60-5 CAPLUS  
 CN Benzoic acid, 3-[(dipropylamino)carbonyl]-5-(2-oxazolyl)-, (1R,2S)-2-amino-3-(3,5-difluorophenyl)-1-[[[3-(2-methylpropyl)-5-thiazolyl)methyl]amino]methyl]propyl ester (9CI) (CA INDEX NAME)

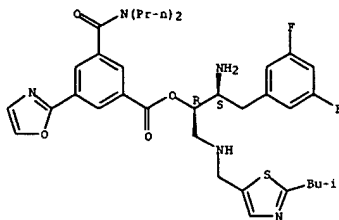
Absolute stereochemistry.



RN 674311-61-6 CAPLUS  
 CN Benzoic acid, 3-[(dipropylamino)carbonyl]-5-(2-oxazolyl)-, (1R,2S)-2-amino-3-(3,5-difluorophenyl)-1-[[[3-ethylphenyl)cyclopropyl]amino]methyl]propyl ester (9CI) (CA INDEX NAME)

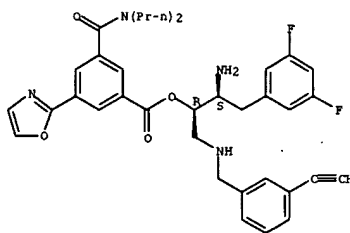
Absolute stereochemistry.

L4 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



RN 674311-51-4 CAPLUS  
 CN Benzoic acid, 3-[(dipropylamino)carbonyl]-5-(2-oxazolyl)-, (1R,2S)-2-amino-3-(3,5-difluorophenyl)-1-[[[3-(3-ethylphenyl)methyl]amino]methyl]propyl ester (9CI) (CA INDEX NAME)

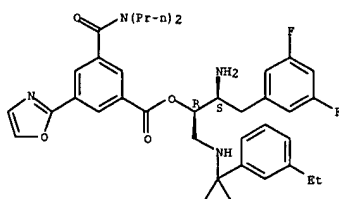
Absolute stereochemistry.



RN 674311-55-8 CAPLUS  
 CN Benzoic acid, 3-[(dipropylamino)carbonyl]-5-(2-oxazolyl)-, (1R,2S)-2-amino-3-(3,5-difluorophenyl)-1-[[[3-(3-ethylphenyl)methyl]amino]methyl]propyl ester (9CI) (CA INDEX NAME)

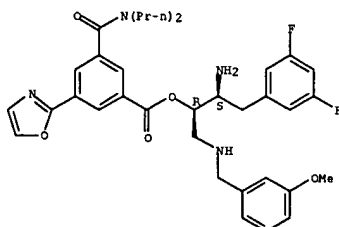
Absolute stereochemistry.

L4 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



RN 674311-64-9 CAPLUS  
 CN Benzoic acid, 3-[(dipropylamino)carbonyl]-5-(2-oxazolyl)-, (1R,2S)-2-amino-3-(3,5-difluorophenyl)-1-[[[3-(3-methoxyphenyl)methyl]amino]methyl]propyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 674311-72-9 CAPLUS  
 CN Benzoic acid, 3-[(dipropylamino)carbonyl]-5-(2-oxazolyl)-, (1R,2S)-2-amino-3-(3,5-difluorophenyl)-1-[[[3-(3-ethylphenyl)methyl]amino]methyl]propyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:412801 CAPLUS

DOCUMENT NUMBER: 139:245782

TITLE: Preparation of N,N'-substituted-1,3-diamino-2-hydroxypropanes for treating Alzheimer's disease  
 Varghese, John; Maillard, Michel; Jagodzinska, Barbara; Beck, James P.; Gailunas, Andrea; Fang, Larry; Sealy, Jennifer; Tenbrink, Ruth; Freskos, John; Mickelson, John; Samala, Lakshman; Hom, Roy

PATENT ASSIGNEE(S): Elan Pharmaceuticals, Inc., USA; Pharmacia & Upjohn Company

SOURCE: PCT Int. Appl., 1243 pp.

CODEN: P1XXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

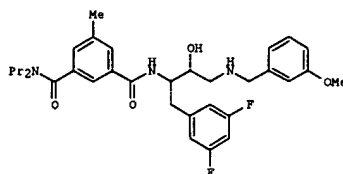
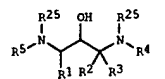
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003040096	A2	20030515	WO 2002-XA36072	20021108
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PRIORITY APPL. INFO.: US 2001-337122P P 20011108				
US 2001-344086P P 20011228				
US 2002-345635P P 20020103				
WO 2002-US36072 A 20021108				

OTHER SOURCE(S): MARPAT 139:245782

GI

L4 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



AB The title compds. [I; R1 = (un)substituted alkyl, alkenyl, alkynyl, etc.; R2 = H, alkyl, haloalkyl, alkenyl, etc.; R3 = H, alkyl, haloalkyl, alkenyl, etc.; or R2 and R3 are taken together with the carbon to which they are attached to form a carbocycle of 3-7 carbon atoms, optionally where one carbon atom is replaced by a heteroatom selected from the group consisting of O, S, SO2, (un)substituted NH; R4 = alkyl, haloalkyl, hydroxyalkyl, etc.; R5 = R6X (wherein X = CO, SO2, (un)substituted CH2; R6 = (un)substituted Ph, naphthyl, indanyl, etc.); R25 = H, alkyl, alkoxy, etc.] which have activity as inhibitors of  $\beta$ -secretase and are therefore useful in treating a variety of disorders such as Alzheimer's disease, were prepared E.g., a multi-step synthesis of (1S,2R)-II, starting from (2S)-2-[(tert-butoxycarbonyl)amino]-3-(3,5-difluorophenyl)propanoic acid, was given. The compds. I showed IC50 of < 20  $\mu$ M in cell free inhibition assay utilizing a synthetic APP substrate. This is a Part 2 of 1-2 series.

IT 597561-61-0P 597561-63-2P 597563-21-0P

597563-22-9P 597563-26-3P 597563-28-5P

597563-29-6P 597563-31-0P 597563-32-1P

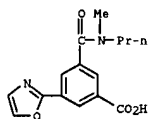
RL: RCT (Reactant); SFN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of N,N'-substituted-1,3-diamino-2-hydroxypropanes for treating Alzheimer's disease)

RN 597561-61-0 CAPLUS

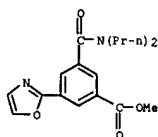
CN Benzoic acid, 3-[(methylpropylamino)carbonyl]-5-(2-oxazolyl)- (9CI) (CA INDEX NAME)

L4 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



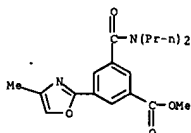
RN 597561-63-2 CAPLUS

CN Benzoic acid, 3-[(dipropylamino)carbonyl]-5-(2-oxazolyl)-, methyl ester (9CI) (CA INDEX NAME)



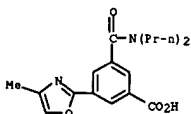
RN 597563-21-8 CAPLUS

CN Benzoic acid, 3-[(dipropylamino)carbonyl]-5-(4-methyl-2-oxazolyl)-, methyl ester (9CI) (CA INDEX NAME)



RN 597563-22-9 CAPLUS

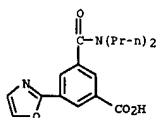
CN Benzoic acid, 3-[(dipropylamino)carbonyl]-5-(4-methyl-2-oxazolyl)- (9CI) (CA INDEX NAME)



L4 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)

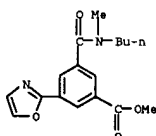
RN 597563-26-3 CAPLUS

CN Benzoic acid, 3-[(dipropylamino)carbonyl]-5-(2-oxazolyl)- (9CI) (CA INDEX NAME)



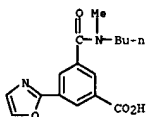
RN 597563-28-5 CAPLUS

CN Benzoic acid, 3-[(butylmethylamino)carbonyl]-5-(2-oxazolyl)-, methyl ester (9CI) (CA INDEX NAME)



RN 597563-29-6 CAPLUS

CN Benzoic acid, 3-[(butylmethylamino)carbonyl]-5-(2-oxazolyl)- (9CI) (CA INDEX NAME)



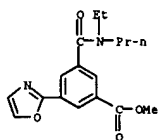
RN 597563-31-0 CAPLUS

CN Benzoic acid, 3-[(ethylpropylamino)carbonyl]-5-(2-oxazolyl)-, methyl ester (9CI) (CA INDEX NAME)



10600100 09/15/05

L4 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)



RN 597563-32-1 CAPLUS  
CN Benzoic acid, 3-[(ethylpropylamino)carbonyl]-5-(2-oxazolyl)- (9CI) (CA  
INDEX NAME)

